Complete Summary

GUIDELINE TITLE

Chronic abnormal uterine bleeding in nongravid women.

BIBLIOGRAPHIC SOURCE(S)

Amann M, Anguino H, Bauman RA, Cheung ML, Harris S, Kennedy J, Kivnick S, Lim A, Moore D, Munro M, Musoke L, Solh S. Chronic abnormal uterine bleeding in nongravid women. Pasadena (CA): Kaiser Permanente Southern California; 2006 Dec. 91 p. [344 references]

GUIDELINE STATUS

This is the current release of the guideline.

The process was designed to be a continuous one, allowing for ongoing modifications and revisions as new higher quality or otherwise clarifying evidence becomes available.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- June 15, 2005, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): U.S. Food and Drug Administration (FDA) recommended proposed labeling for both the prescription and over the counter (OTC) NSAIDs and a medication guide for the entire class of prescription products.
- April 7, 2005, Non-steroidal anti-inflammatory drugs (NSAIDS) (prescription and OTC, including ibuprofen and naproxen): FDA asked manufacturers of prescription and non-prescription (OTC) non-steroidal anti-inflammatory drugs (NSAIDs) to revise their labeling to include more specific information about potential gastrointestinal (GI) and cardiovascular (CV) risks.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic abnormal uterine bleeding in nongravid women

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Pathology
Radiology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To develop evidence based consensus guidelines for the management of women with chronic abnormal uterine bleeding in the reproductive years

TARGET POPULATION

Women with chronic abnormal uterine bleeding in the reproductive years

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Assessment

1. Risk assessment

2. Sequencing of investigations
3. Clinical investigation
4. Physical exam
5. Complete blood count (CBC)
6. Blood or urine pregnancy test
7. Structured history to screen for inherited systemic disorders of hemostasis
8. Assessment of ovulatory function
9. Measurement of thyroid function
10. Uterine cavity assessment
    - Endometrial biopsy
    - Transvaginal sonography (TVS)
    - Saline infusion sonography (SIS)
    - Hysteroscopy

Treatment/ Management

1. Oral iron therapy
2. Medical therapy options
    - Ovulatory dysfunctional uterine bleeding (DUB) (Nonsteroidal anti-inflammatory agents, combination oral contraceptives, oral progestins either continuously or nearly continuously, local progestins as administered via a progestin secreting intrauterine contraceptive device, antifibrinolytics, depot gonadotropin releasing hormone [GnRH] agonists, Danazol, oral or transvaginal)
    - Anovulatory DUB (lifestyle modification including stress reduction and weight loss, progestins administered cyclically, continuously or nearly continuously, combination oral contraceptives, GnRH agonists [in select women])
3. Surgical therapy options:
    - Endometrial ablation
    - Resectoscopic myomectomy
    - Abdominal myomectomy
    - Uterine artery embolization/occlusion
    - Myolysis
    - Hysterectomy
4. Follow-up

MAJOR OUTCOMES CONSIDERED

- Incidence of dysfunctional uterine bleeding
- Sensitivity and specificity of diagnostic tests
- Side effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature searches were performed in MEDLINE and the Cochrane Database of systematic reviews using the following search terms: chronic uterine bleeding; heavy menstrual bleeding, menorrhagia, dysfunctional uterine bleeding, leiomyomas (and myomas) therapy; investigation; diagnosis, therapy, endometrial ablation. Also searched were the websites of the American College of Obstetricians and Gynecologists, the Society of Obstetricians and Gynecologists of Canada, the New Zealand Guidelines Group, the Royal College of Obstetricians and Gynecologists, and the Geneva Foundation for Medical Education and Research, (http://www.gfmer.ch/000_Homepage_En.htm) each a repository of web-published guidelines. The date of the last search was June 30, 2005.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of Evidence

Modified US Preventive Services Task Force Hierarchy of Research Design

I-1: Evidence obtained from at least one meta analysis or systematic review of randomized clinical trials.

I-2: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Descriptive studies and case reports.

IV: Opinions of respected authorities, consensus committees, clinical experience

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The guideline was developed using the available evidence and a consensus process. Evidence was classified using a modification of the system adopted by the U.S Preventive Services Task Force of the Agency for Health Research and Quality (AHRQ) (See Appendix I in the original guideline document) adding a subgroup for Class I evidence to allow for metaanalysis of randomized controlled trials, such as a Cochrane review. An additional modification was to create a Class IV grouping that isolated expert opinion, including that from guidelines or other consensus documents from national or international organizations or from the collective opinion of the members of the Abnormal Uterine Bleeding Working Group (AUBWG) itself.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Chair of the Committee was selected by the Regional Chief of Obstetrics and Gynecology for Kaiser Permanente Southern California. The remaining members of the Committee were selected by the chairs of each of the 12 medical centers. Face to face meetings were held monthly with ad hoc face to face or teleconference-based meetings held as necessary. After an introductory discussion on the general and Southern California Permanente Medical Group (SCPMG)-specific issues involved in the general problem of chronic uterine bleeding, the committee met as a whole to review methods of guideline development, agree on terms for evidence classification, and to come to consensus on the scope of the guideline(s) to be developed. The Working Group Chair prepared a shell document to aid the guideline development process.

A subgroup of three individuals was charged with leading the investigation and developing draft documents for meetings of the whole group. Drafts were electronically distributed to the whole group and monthly face to face meetings were used to obtain feedback from each of the members of the committee.

The recommendations were created and classified according to the strength of the evidence, classified according to the system used by the American College of Obstetricians and Gynecologists (see rating scheme below).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Support for Recommendations

Based on the American College of Obstetricians and Gynecologists Strength of Recommendation Classification:

Level A. Recommendations are based on good and consistent scientific evidence

Level B. Recommendations are based on limited or inconsistent scientific evidence

Level C. Recommendations are based primarily on consensus and expert opinion

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The consensus document was created, approved by the members of the Abnormal Uterine Bleeding Working Group (AUBWG) on November 30, 2004 and then submitted to the Southern California Regional Chiefs for review, comment, and approval.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of evidence (**I-1 – IV**) and levels of recommendations (**A-C**) are defined at the end of the "Major Recommendations" field.

Guideline Candidates (both must be present)

- Reproductive aged women who are not pregnant
    - Abnormal uterine bleeding that is one or a combination of the following
        - Irregular (unpredictable timing; e.g., every(q) 21 to 60 days)
        - Bleeding between predictable periods ("metrorrhagia")
        - Heavy, predictable onset, normal cycle length (q 22 to 35 days)
            - Excessive volume (Heavy menstrual bleeding; menorrhagia)
            - Excessive duration (Heavy menstrual bleeding; menorrhagia)
        - Heavy, predictable onset, abnormal normal cycle length
            - Too frequent (cycle length < 22 days)("polymenorrhea")
            - Too infrequent (cycle length >35 days)("oligomenorrhea")

General Investigation of Reproductive Aged Women with Chronic Abnormal Uterine Bleeding (AUB)

- All patients with chronic AUB should be considered for a complete blood count (CBC). **(Level C)**
- All patients presenting with chronic AUB should be evaluated for pregnancy, if necessary with a blood or urine pregnancy test. **(Level C)**
- Women with heavy uterine bleeding should have a structured history to screen for inherited systemic disorders of hemostasis. **(Level A)** (see Table 1 below)
- Each patient with chronic AUB should be assessed for ovulatory function which can be reliably confirmed with a history of predictable, cyclic mense with a cycle length of every 22 to 35 days. **(Level C)**
- Measurement of thyroid function with TSH is appropriate in women with suspected or known anovulatory dysfunctional uterine bleeding (DUB). Further investigation of endocrinopathy should be performed in conjunction with a gynecologist. **(Level C)**

Table 1: Screening for an underlying disorder of hemostasis in the patient with excessive menstrual bleeding*

Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding should be by a structured history:
1. Heavy menstrual bleeding since menarche
2. One of the following: a. Post-partum hemorrhage b. Surgical related bleeding c. Bleeding associated with dental work
3. Two or more of the following symptoms: a. Bruising 1-2 times/month b. Epistaxis 1-2 times/month c. Frequent gum bleeding d. Family history of bleeding symptoms

A positive screen comprises any of the following (1) heavy bleeding since menarche, one from list (2) or two or more from list (3). Patients with a positive screen should be considered for further evaluation including consultation with a hematologist and/or testing of von Willebrand factor and Ristocetin cofactor.

*From Kadir RA, Economides DL, Sabin CA, Owens D, Lee CA. Frequency of inherited bleeding disorders in women with menorrhagia. Lancet 1998; 351:485-9.

Uterine Cavity Assessment

- The goals for evaluation of the endometrial cavity in women with chronic abnormal uterine bleeding (AUB) include (1) Detection of endometrial hyperplasia or cancer in selected patients, and (2) Identification of focal lesions such as polyps and leiomyomas which might explain the patient's bleeding. **(Level C)**
- Evaluation of the Endometrium

- When endometrial sampling is indicated in premenopausal women with AUB, outpatient endometrial biopsy with catheter techniques should be considered the first line approach. **(Level A)**
- When there is an increased risk of endometrial hyperplasia or neoplasia, endometrial sampling should be performed. **(Level A)** Such circumstances include the following:
    - Over the age of 40. **(Level B)**
    - Women less than forty with risk factors judged sufficient to warrant biopsy. These include features suggestive of chronic anovulation (irregular menses, infertility); and weight greater than 90 Kg. **(Level B)**
    - Patients with a family history of hereditary nonpolyposis colorectal cancer syndrome (Lynch Syndrome [see Appendix IV in the original guideline document]) **(Level B)**
- If the endometrial biopsy is indicated and cannot be obtained or is inadequate, repeat sampling should be attempted, if necessary with Dilation and Curettage (D&C). Patients taken to the operating room should have hysteroscopic evaluation prior to endometrial sampling and it is preferable that the surgeon be prepared to remove identified lesions under hysteroscopic guidance. **(Level C)**
- If chronic AUB continues despite normal and satisfactory endometrial sampling, the patient should be considered for further evaluation with ultrasound, saline infusion sonography (SIS), and or hysteroscopy. **(Level A)**

- Transvaginal Sonography (TVS)
    - In general, patients should not be sent to radiology for pelvic ultrasounds prior to evaluation by gynecology. Office ultrasound should be done by a gynecologist (or other practitioner) with training in office ultrasound techniques. **(Level C)**
    - Routine ultrasonography is generally unnecessary for initial visits but should be considered in any individual with persisting symptoms and especially those who fail initial medical therapy. **(Level C)**
    - An ultrasound scan is deemed adequate if it demonstrates the entire endometrial echo in the longitudinal and transverse planes through the widest part of the endometrial cavity. **(Level C)**
    - There is no consensus on the upper limit of endometrial thickness in premenopausal women, in part because the thickness varies with the normal systemic variation in ovarian gonadal steroids. **(Level B)**
- Evaluation of Endometrial Cavity Structure
    - Evaluation for structural causes of (abnormal uterine bleeding) AUB is most reliably determined by hysteroscopy and/or diagnostic imaging techniques (e.g., transvaginal ultrasonography or saline infusion sonography). **(Level A)**
    - Transvaginal ultrasound is a good screening test but may miss some focal lesions such as polyps. **(Level B)**
    - Irregular thickening of the endometrium (as seen by ultrasound) suggests the presence of one or more focal lesions. When such irregularity exists, when the endometrial cavity cannot be identified in its entirety or, if for any other reason polyps or fibroids involving the endometrial cavity are suspected, further evaluation should include either saline infusion sonography (SIS) or hysteroscopy. **(Level A)**

- All women with excessive bleeding secondary to chronic AUB should be offered oral iron therapy. **(Level C)**
- Ovulatory DUB (cyclical heavy bleeding unrelated to structural abnormalities): Medical therapy options. (Note: women with DUB may have asymptomatic lesions such as intramural or subserosal fibroids)
    - Nonsteroidal anti-inflammatory agents. **(Level A)**
    - Combination oral contraceptives **(Level C)**
    - Oral progestins either continuously or nearly continuously. **(Level C)**
    - Local progestins as administered via a progestin secreting intrauterine contraceptive device. **(Level A)**
    - Antifibrinolytics **(Level A)** (currently not readily available in the US)
    - Depot GnRH agonists (for limited duration). **(Level C)**
    - Danazol, oral or transvaginal. **(Level A)**
- Anovulatory DUB (irregular and unpredictable bleeding unrelated to structural abnormalities): Medical therapy options: (Note: women with DUB may have asymptomatic lesions such as intramural or subserosal fibroids)
    - Lifestyle issues including stress reduction and weight loss may be important in the management of AUB associated with an anovulatory state. **(Level C)**
    - Progestins administered cyclically. **(Level B)**
    - Progestin administered continuously or nearly continuously. **(Level B)**
    - Combination oral contraceptives. **(Level B)**
    - The role of metformin and other hypoglycemic agents for the routine treatment of chronic anovulatory AUB has not been established. **(Level B)**
    - Ovulation induction is not indicated as therapy for anovulatory DUB. **(Level C)**
    - GnRH agonists may have a role in the management of selected women with chronic anovulatory AUB. **(Level B)** Such management should only be offered following consultation with a gynecologist.
- Persistent AUB: If AUB persists after a negative endometrial biopsy and appropriate medical therapy, the endometrial cavity should be assessed if not previously evaluated.
- Surgical therapy for women with chronic DUB is currently reserved for women not interested in future fertility. **(Level C)**
    - Patients taken for surgery for chronic AUB should have preoperative complete blood count (CBC) adequate screening for coagulopathy (See Table 1 above) and appropriate assessment of the endometrium and endometrial cavity. **(Level C)**
    - Endometrial ablation is frequently effective for chronic DUB and can be performed by outpatient resectoscopic or non-resectoscopic techniques which have equal efficacy when used by well trained and experienced surgeons. **(Level A).**
    - Hysterectomy is a surgical option for women with chronic DUB.
- Surgical Options for Women with Chronic AUB Associated with Leiomyomas and Polyps
    - Symptomatic endometrial polyps should be completely removed under hysteroscopic direction. **(Level B)**
    - The surgical management of AUB secondary to leiomyomas is determined by the size, location and number of the myomas as well as the patient's desires regarding future fertility. **(Level C)**
    - Endometrial Ablation: Selected patients with leiomyoma-related AUB who do not wish to retain fertility may be considered for endometrial

ablation with a resectoscope or non-resectoscopic device demonstrated effective in the presence of submucous leiomyomas. **(Level A)**

- Resectoscopic myomectomy
    - Resectoscopic myomectomy should be offered to patients with type 0, I, and selected type II myomas (see Appendix V in the original guideline document) particularly those who wish to retain fertility. **(Level C)**
    - Resectoscopic myomectomy should be performed with an accurate system and protocol for measuring and managing systemic absorption of distention media. **(Level A)**
    - In some instances, and particularly with multiple submucous leiomyomas, staged resectoscopic removal may be appropriate. **(Level B)**
    - Women with submucosal leiomyomas greater than 5 cm in diameter should be considered for alternate methods of removal. **(Level C)**
- Abdominal myomectomy is the preferred procedure for women with AUB related to myomas unsuitable for resectoscopic removal and who wish to retain their uterus. **(Level C)**
- Uterine Artery Embolization/Occlusion
    - Radiologic uterine artery occlusion may be offered to women with chronic AUB associated with uterine leiomyomata. **(Level A)**
    - Although successful pregnancies have occurred following uterine artery embolization (UAE), the role for this procedure in women who wish to preserve fertility has not been established. **(Level B)**
- Myolysis is an investigational procedure for the in situ treatment of uterine leiomyomas with radiofrequency electrosurgery, cryotherapy, or focused ultrasound. It does not appear to be appropriate for women who desire future fertility. **(Level B)**

- Hysterectomy for Women with Chronic AUB

  If hysterectomy (total or subtotal) is to be performed for AUB it should be done by the least invasive technique within the capabilities of the surgeon. **(Level A)**

Definitions:

Support for Recommendations

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III: Descriptive studies and case reports.

IV: Opinions of respected authorities, consensus committees, clinical experience

CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the original guideline document, titled:

- Chronic Abnormal Uterine Bleeding (AUB) Investigation
- Chronic Dysfunctional Uterine Bleeding (DUB) Therapy
- Chronic Abnormal Uterine Bleeding (AUB) Therapy - Secondary to Benign Target Lesions (Wishes to retain uterus not fertility)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and management of abnormal uterine bleeding

POTENTIAL HARMS

- False negative or positive investigative test results
- Side effects of treatment

CONTRAINDICATIONS

CONTRAINDICATIONS

Rapid growth of apparent myomas in post menopausal women is likely a contraindication to conservative surgical procedures like myomectomy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The recommendations in this guideline are for informational purposes only. They are not intended nor designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners, considering each patient's needs on an individual basis. Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Amann M, Anguino H, Bauman RA, Cheung ML, Harris S, Kennedy J, Kivnick S, Lim A, Moore D, Munro M, Musoke L, Solh S. Chronic abnormal uterine bleeding in nongravid women. Pasadena (CA): Kaiser Permanente Southern California; 2006 Dec. 91 p. [344 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Dec

GUIDELINE DEVELOPER(S)

Kaiser Permanente-Southern California - Managed Care Organization

SOURCE(S) OF FUNDING

Kaiser Permanente Southern California

GUIDELINE COMMITTEE

Southern California Permanente Medical Group, Abnormal Uterine Bleeding Working Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Clinical Lead: Malcolm Munro, MD (*Chair*)

Kaiser Permanente Southern California Abnormal Uterine Bleeding Working Group Members: Michael Amann, MD; Hector Anguino, MD; Roselie A. Bauman, MD; Mon-Lai Cheung, MD; Selena Harris, MD; John Kennedy, MD; Seth Kivnick, MD; Aaron Lim, MD; Damien Moore, MD; Lois Musoke, MD; Saad Solh, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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The process was designed to be a continuous one, allowing for ongoing modifications and revisions as new higher quality or otherwise clarifying evidence becomes available.

GUIDELINE AVAILABILITY

Electronic copies: Available from Marguerite Koster, Practice Leader, Technology Assessment and Guidelines Unit, Kaiser Permanente Southern California; Email: Marguerite.A.Koster@kp.org

Print copies: Available from Malcolm G. Munro, MD, FRCS(c), FACOG, Department of Obstetrics and Gynecology, Kaiser Permanente Southern California, Professor, Department of Obstetrics & Gynecology, David Geffen School of Medicine at UCLA; Email: M.G.Munro@kp.org

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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